

### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims:**

Claims 1-167 (Canceled without prejudice).

168. (Currently amended): A kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment or fragments in a material taken or gathered from an individual, said kit comprising a binding agent capable of binding ~~[[said]]~~ a plasma thrombospondin fragment or plasma thrombospondin fragments and/or a portion of said plasma thrombospondin fragment or plasma thrombospondin fragments, each of said plasma fragment or plasma thrombospondin fragments being one that starts between amino acyl residues I-165 and V-263, inclusive, and ends between amino acyl residues R-792 and Y-982, inclusive, each of said plasma thrombospondin fragment, fragments or portion being at least 20 kDa in size wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, said kit further comprising a reference molecule, said reference molecule being selected from the group consisting of a thrombospondin fragment, a derivatized thrombospondin fragment, a peptide derived from a thrombospondin fragment and a derivatized peptide derived from a thrombospondin fragment, said fragment or peptide corresponding to or within the region of thrombospondin extending from amino acyl residues I-165 to Y-982, said reference molecule

capable of binding to the binding agent, and wherein I-165, V-263, R-792, and Y-982 refer to residues 183, 281, 810, and 1000, respectively of SEQ ID NO:38.

169. (Currently amended): A kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment or fragments in a material taken or gathered from an individual, said kit comprising a binding agent capable of binding ~~[[said]]~~ a plasma thrombospondin fragment or plasma thrombospondin fragments, each of said plasma thrombospondin fragment or plasma thrombospondin fragments having a molecular weight not exceeding 110 kDa, wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, and wherein the plasma thrombospondin fragment or each of the plasma thrombospondin fragments comprises a region of thrombospondin, said region selected from the group of regions consisting of:

a domain or a portion thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, ~~[[an oligomerization domain,]]~~ a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat; and

~~[[a portion of]]~~ a collagen type V binding domain a or portion thereof, ~~[[; and~~

~~an epitope for binding the TSP Ab-4 antibody]]~~ and wherein the binding agent specifically binds to an epitope within said region, said kit further comprising a reference molecule, said reference molecule being selected from the group consisting of a thrombospondin fragment, a derivatized thrombospondin fragment, a peptide derived from a thrombospondin fragment and a derivatized peptide derived from a thrombospondin fragment, said fragment or

peptide corresponding to all or a portion of one or more regions selected from said group of regions, said reference molecule capable of binding to the binding agent.

170. (Currently amended): A kit of Claim 169 wherein the region of thrombospondin is a domain or a portion thereof within the protease-resistant core of thrombospondin, said domain being selected from the group of regions consisting of a domain of inter-chain disulfide bonds, ~~[[an oligomerization domain,]]~~ a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat, the fragment or peptide corresponding to all or a portion of one or more regions selected from said group, said reference molecule capable of binding to the binding agent.

171. (Currently amended): A kit of Claim 169 wherein the region of thrombospondin is ~~[[a portion of]]~~ a collagen type V binding domain the fragment or peptide corresponding to all or a portion of the collagen type V binding domain.

172 - 176. (Canceled without prejudice).

177. (Currently amended): A kit of ~~[[Claim 176]]~~ Claims 168, 189, 170 or 171 wherein the sequence of the reference molecule comprises the sequence TEENKE (SEQ ID NO:1).

178-179. (Canceled without prejudice).

180. (Currently amended): A kit of Claim 177 wherein the binding agent capable of binding the plasma thrombospondin fragment or plasma thrombospondin fragments is a first binding agent and said kit further comprises a second binding agent, said second binding agent capable of binding thrombospondin but not the plasma thrombospondin fragment or plasma thrombospondin fragments.

Claims 181-182. (Canceled without prejudice).

183. (New): A kit comprising a first binding agent and a second binding agent, said first

binding agent capable of a binding thrombospondin fragment or fragments in the plasma of an individual or in a material taken from the plasma of an individual, said second binding agent capable of binding thrombospondin but not the thrombospondin fragment or fragments in the plasma of the individual.

184 (New): A kit of Claim 183 wherein the first binding agent is capable of binding to a thrombospondin fragment, in the plasma of an individual, that is within a molecular weight range selected from the group consisting of 80 to 110 kDa, 40 to 60 kDa, and 20 to 35 kDa, wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction.

185 (New): A kit of Claim 183 wherein the first binding agent is capable of binding to a thrombospondin fragment, in the plasma of an individual, that is at least 20 kDa in size but does not exceed 110 kDa in size; wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction.

186 (New): A kit of Claim 183 wherein the first binding agent is capable of binding to a thrombospondin fragment, in the plasma of an individual, that is at least 20 kDa in size but does not exceed 35 kDa in size; wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction.

187 (New): A kit of Claim 183 wherein the first binding agent is capable of binding to a thrombospondin fragment, in the plasma of an individual, that starts between amino acyl residues I-165 and V-263, inclusive, and ends between amino acyl residues R-792 and Y-982, inclusive, said plasma thrombospondin fragment being at least 20 kDa in size wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, and wherein I-165, V-263, R-792, and Y-982 refer to residues 183, 281, 810, and 1000, respectively of SEQ ID NO:38.

188 (New): A kit of Claim 183 wherein the first binding agent is capable of binding to a thrombospondin fragment, in the plasma of an individual, that has a molecular weight not exceeding 110 kDa, wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, and wherein the plasma thrombospondin fragment comprises a region of thrombospondin, said region selected from the group of regions consisting of:

a domain or a portion thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat; and

a collagen type V binding domain a or portion thereof,

and wherein the binding agent specifically binds to an epitope within said region.

189. (New): A kit of Claim 183 wherein the kit further comprises a reference molecule selected from the group consisting of a reference molecule capable of binding to the first binding agent and a reference molecule capable of binding to the second binding agent.

190. (New): A kit of Claim 187 said kit further comprising a reference molecule, said reference molecule comprising a thrombospondin fragment corresponding to or within the region of thrombospondin extending from amino acyl residues I-165 to Y-982, said reference molecule capable of binding to the binding agent.

191. (New): A kit of Claim 188 said kit further comprising a reference molecule, said reference molecule comprising a thrombospondin fragment consisting of all or a portion of one or more regions selected from said group of regions, said reference molecule capable of binding to the binding agent.

192. (New): A kit of Claims 168, 169, 170, or 171 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the group consisting of a device for separation of plasma, heparin, a heparin fragment, a protease inhibitor, a platelet inhibitor, and a clotting inhibitor.

193. (New): A kit of Claims 168, 169, 170, or 171 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the group consisting of heparin, a heparin fragment, a protease inhibitor, a platelet inhibitor, and a clotting inhibitor.

194. (New): A kit of Claims 168, 169, 170, or 171 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the group consisting of a device for separation of plasma.

195. (New): A kit of Claims 168, 169, 170, 171, 177, 192, 193 or 194 wherein the binding agent is an antibody.

196. (New): A kit of Claims 180, 183, 184, 185, 186, 187, 188, 189, 190 or 191 wherein the first binding agent is an antibody and the second binding agent is an antibody.

197. (New): A kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment or fragments in a material taken or gathered from an individual, said kit comprising a binding agent capable of binding a plasma thrombospondin fragment or plasma thrombospondin fragments and/or a portion of said plasma thrombospondin fragment or plasma thrombospondin fragments, each of said plasma fragment or plasma thrombospondin fragments being one that starts between amino acyl residues I-165 and V-263, inclusive, and ends between amino acyl residues R-792 and Y-982, inclusive, each of

said plasma thrombospondin fragment, fragments or portion being at least 20 kDa in size wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, said kit further comprising a reference molecule, said molecule comprising a target to which the binding agent binds, said target being one that is present in a plasma thrombospondin fragment, said reference molecule selected from the group consisting of a thrombospondin fragment, a derivatized thrombospondin fragment, a peptide derived from a thrombospondin fragment, and a derivatized peptide derived from a thrombospondin fragment, and wherein I-165, V-263, R-792, and Y-982 refer to residues 183, 281, 810, and 1000, respectively of SEQ ID NO:38.

198. (New): A kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment or fragments in a material taken or gathered from an individual, said kit comprising a binding agent capable of binding a plasma thrombospondin fragment or plasma thrombospondin fragments, each of said plasma thrombospondin fragment or plasma thrombospondin fragments having a molecular weight not exceeding 110 kDa, wherein the size in kDa is that determined by gel electrophoresis after disulfide bond reduction, and wherein the plasma thrombospondin fragment or each of the plasma thrombospondin fragments comprises a region of thrombospondin, said region selected from the group of regions consisting of:

a domain or a portion thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat; and

a collagen type V binding domain or a portion thereof;

and wherein the binding agent specifically binds to an epitope within said region, said kit further comprising a reference molecule, said molecule comprising a target to which the binding agent binds, said target being one that is present in a plasma thrombospondin fragment, said reference molecule selected from the group consisting of a thrombospondin fragment, a derivatized thrombospondin fragment, a peptide derived from a thrombospondin fragment, and a derivatized peptide derived from a thrombosponding fragment.

199. (New): A kit of Claim 198 wherein the region of thrombospondin is a domain or a portion thereof within the protease-resistant core of thrombospondin, said domain being selected from the group of regions consisting of a domain of inter-chain disulfide bonds, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat.

200. (New): A kit of Claim 198 wherein the region of thrombospondin is a collagen type V binding domain or a portion thereof.

201. (New): A kit of Claims 197, 198, 199 or 200 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the group consisting of a device for separation of plasma, heparin, a heparin fragment, a protease inhibitor, a platelet inhibitor, and a clotting inhibitor.

202. (New): A kit of Claims 197, 198, 199 or 200 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the group consisting of heparin, a heparin fragment, a protease inhibitor, a platelet inhibitor, and a clotting inhibitor.

203. (New): A kit of Claims 197, 198, 199 or 200 wherein said kit further comprise a means for minimizing platelet activation and/or protease activity said means selected from the



group consisting of a device for separation of plasma.

204. (New): A kit of Claims 197, 198, 199, 200, 201, 202, or 203 wherein the binding agent is an antibody.

205. (New) A kit of Claims 168, 169, 170, 171, 177, 192, 193, 194, 197, 198, 199, 200, 201, 202, or 203 where the reference molecule is selected from the group consisting of a thrombospondin fragment and a peptide derived from a thrombospondin fragment.

206. (New): A kit of Claim 205 wherein the binding agent is an antibody.